



PALLIATIVE CARE CASE OF THE MONTH

“Treating depression in patients who can’t take oral medications”

by

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Case: The patient is a 57-year-old man with several gunshot wounds to the abdomen and chest whom the specialist palliative care team was asked to see for pain and depression. The patient’s hospital course was complicated by multiple GI fistulae and abscesses, and for the last month he has been NPO, on TPN and not allowed to eat or drink anything.

When we first saw him, he was on 150 mcg of Fentanyl and getting rare prn doses of hydromorphone. He did not complain of pain. He acknowledged that he was quite depressed, had anhedonia and was not sure anything could make it better. He spent all day in bed, often with the lights off and the sheets over his head. He had no suicidal ideation. He was not interested in music therapy, pet therapy, a pastor or a volunteer. He had no past medical history of depression. Because he was NPO, he was not on an antidepressant.

Other than his lack of poor eye contact and his multiple abdominal drains with an open abdominal pouch, his physical exam was unremarkable. He had previously had normal B12 and TSH, and his other laboratory results were consistent only with mild malnutrition and chronic inflammation due to the abdominal abscesses.

In talking to his significant other, she also felt that the patient was severely depressed and wondered if we could do anything to improve the quality of his life during his hospital stay (which was expected to be weeks to months if one included long-term care).

Discussion: Traditionally, antidepressants are delivered as a tablet or less frequently in a liquid form. But in this case, oral antidepressants are not possible. The question is what to do.

First, one must consider non-pharmacologic treatments that are possible. Psychotherapy is effective for the initial treatment of major depression based on numerous randomized controlled trials.¹ While the best evidence is for cognitive behavioral therapy, in seriously ill patients existential therapies such as dignity therapy, meaning-centered therapy and therapeutic life review have been used.² In all patients, psychotherapy is effective in roughly 40% of the patients (as opposed to 20% with placebo³).

Electroconvulsive therapy has also been successfully used in medically ill patients, but the data is sparse in patients as seriously ill as above.⁴ In addition, transport to and from ECT would have been quite difficult, and his abdominal drains may have precluded this option.

Alternatives to administering oral antidepressants exist but relatively little is known about them. There are case reports of intravenous, buccal, sublingual, transdermal and rectal administration of antidepressants. For example, outside of America intravenous citalopram, mirtazapine and amitriptyline have been used with good tolerability. There is minimal data regarding efficacy.

Similarly, there is data for topical doxepin, a drug that while available in the United States is only FDA approved for pruritis. Transdermal selegilan is FDA approved for the use in depression; however, it is a MAO inhibitor which most doctors do not have experience using. Because it has multiple drug-drug and food-drug interactions (particularly tyrosine rich foods) which may result in severe side effects (eg. Hypertensive crisis), if someone wishes to use this drug. A psychiatric consultation is recommended.⁵⁻⁷

Two newer formulations also have been: 1) Sublingual mirtazapine in the form of an orally dissolving tablet (ODT) which still requires an intact gastrointestinal system, but is allowed to be used in patients who are otherwise NPO. 2) Intravenous ketamine which has limited but increasing data.

Mirtazapine is an established antidepressant with well-documented efficacy in controlled clinical trials. It has a dual mechanism of action: working both by antagonizing the adrenergic alpha-2 autoreceptors and alpha-2 heteroreceptors and blocking 5HT₂ and 5HT₃ receptors. The orally disintegrating caplet is placed under the tongue and requires no fluid other than one’s saliva for absorption. The extent and rate of absorption of mirtazapine is not affected by food, which may be helpful in NPO patients. In one prospective open-labeled, multicenter study in patients with mild to severe depression in outpatient mental health clinics, patients were given ODT and oral mirtazapine and had significant improvement in their depression. More importantly, the vast majority (80%) preferred the oral dissolving tablet to the oral formulation of mirtazapine. The most frequent adverse effects were weight gain, sedation (particularly at a lower dose), dizziness and dry mouth. The cost of the ODT mirtazapine is roughly \$80.00 for thirty 45 mg pills⁸⁻⁹

Ketamine is an anesthetic drug that has also been used off label for depression. The drug has been shown to be effective in multiple small, randomized, controlled trials of IV ketamine depression, even when the patient has antidepressant refractory major depressive disorders. Interestingly, it is different from conventional antidepressants in that the antidepressant benefits are seen within hours of administration, peak after a day and are lost within three days to two weeks. There is limited data on long-term use, although there are case series of 2 or 3-week course of ketamine delivered 2 or 3 times per week, followed by a taper period and/or continued treatments based on empirically determined duration of responses for each patient. Adverse effects include drowsiness, dizziness, poor coordination, blurred vision and feelings of strangeness or unreality. In addition, some patients have hemodynamic abnormalities with transient mean increases in systolic and diastolic blood pressure of 20 mm of mercury and 13 mm of mercury respectively. In some case-controlled series, patients have benefited from repeated intravenous doses, and there are also case series of patients receiving oral ketamine after intravenous doses.

Personal details in the case published have been altered to protect patient privacy.

For palliative care consultations please contact the Supportive and Palliative Care programs at PUH/MUH, 647-7243, pager # 8511, Shadyside, 647-7243, pager # 8513, Perioperative/Trauma Pain, 647-7243, pager # 7246, UPCI Cancer Pain Service, pager 644-1724, Interventional Pain 784-4000, Magee Women’s Hospital, pager 412-647-7243 pager # 8510, VA Palliative Care Program, 688-6178, pager # 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children’s pager 958-3844.

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(Discussion Continued)

Ketamine is very inexpensive, although in many hospitals there are costs associated with increased hemodynamic monitoring.¹⁰⁻¹²

These results are encouraging, particular for depressed NPO patients in whom psychotherapy is not an option either because of the lack of therapists or because of the length of time that they will be in the hospital. However, the data is sparse enough and the side effects are significant enough that a psychiatric consultation is recommended for patients who cannot receive oral antidepressants.

Case Follow-up: A psychologist was asked to see him, and his lack of involvement made treatment difficult. We tried ODT mirtazapine which the patient disliked and often refused. With probing we discovered he wasn't making adequate saliva, the ODT did not dissolve and the tablet just sat in his mouth for hours at a time.

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